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September 20, 2004

SENT BY FACSIMILE WITH CONFIRMATION BY COURIER

Our File : 16579

European Patent Office
D-80298 Munich
GERMANY

Attention: **International Preliminary Examining Authority**
(Authorized Officer: Clement, S.)

Dear Sirs:

Applicant: **Ottawa Health Research Institute, National Research Council of Canada, et al.**
Appln. No.: **PCT/CA03/001180**
Title: **"Bio-Synthetic Matrix and Uses Thereof"**

This is in response to the Written Opinion dated May 18, 2004. The initial due date for responding to this Written Opinion was August 18, 2004, however, a one month extension of time for responding to this Written Opinion was requested on August 18, 2004. As we have not received any indication that this request was not granted, we have assumed that the Response to this Written Opinion was due on September 18, 2004.

In accordance with Rule 80.5 PCT, since September 18, 2004 fell on a Saturday and today, September 20, 2004 is the next subsequent business day, this Response to the Written Opinion should be considered to be timely filed.

Article 34 Amendments

In accordance with Article 34 PCT, please amend the present application as follows:

In the claims:

In claim 1, line 4, replace "polymer" with --co-polymer-- and after "1,000,000" insert --, wherein said synthetic co-polymer is reactive with primary amines via the pendant cross-linkable moiety--.

Add new claims 51 – 110.

Claim pages 50 and 58 – 64, incorporating the above amendments, are submitted herewith.

Remarks

The Applicant has amended the claim 1 and added claims 51 – 110 in order to more clearly and precisely define the invention. No new matter has been added by way of the present amendments.

The Examiner has objected to previously pending claim 1 as lacking novelty under Article 33(2) PCT. Specifically, the Examiner has suggested that the subject matter of claim 1 was previously disclosed in International Application No. WO 01/32730.

As noted by the Examiner, WO 01/32730 discloses an implantable biological device comprising an amphiphilic network membrane. The disclosed amphiphilic network membrane is formed from a hydrophobic (not hydrophilic as noted by the Examiner) cross-linking agent and hydrophilic co-monomers. The hydrophobic cross-linking agent is a telechelic three-arm polyisobutylene having acrylate or methacrylate end caps, wherein, according to the Examiner, two (meth)acrylic acid groups can be considered to be "pendant cross-linkable moieties." These cross-linkable moieties are used to react with the hydrophilic monomers to form the amphiphilic network membrane as illustrated in Figure 1 of WO 01/32730. The disclosed amphiphilic network membrane does not contain free (meth)acrylic acid groups that are reactive with primary amines.

In contrast to the amphiphilic network membrane of WO 01/32730, the presently claimed synthetic co-polymer is reactive with primary amines via the pendant cross-linkable moiety. The copolymerization of components of the synthetic polymer does not involve cross-links forming with the pendant cross-linkable moiety. Rather, the synthetic polymer is designed to maintain free cross-linkable moieties in order to facilitate production of a hydrogel by forming cross-links with primary amino groups of a bio-polymer. Therefore, the Applicant submits that the subject matter of amended claim 1 is not anticipated by WO 01/32730.

In view of the foregoing comments and claim amendments, the Applicant respectfully requests issuance of a favourable International Preliminary Examination Report.

Yours very truly,

Stephanie R. White, Ph.D.
Patent Agent

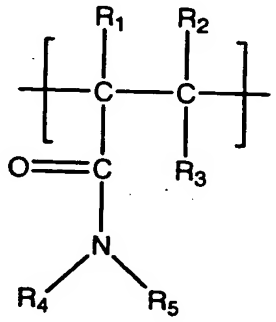
SRW:bw
Enclosure

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A synthetic co-polymer comprising one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer, one or more hydrophilic co-monomer and one or more acryl- or methacryl- carboxylic acid co-monomer derivatised to contain a pendant cross-linkable moiety, said synthetic co-polymer having a number average molecular mass between about 2,000 and about 1,000,000, wherein said synthetic co-polymer is reactive with primary amines via the pendant cross-linkable moiety.

2. The synthetic co-polymer according to claim 1, wherein:

(a) said N-alkyl or NN-dialkyl substituted acrylamide co-monomer has a structure of Formula I:

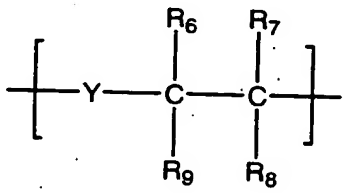


I

wherein:

R_1, R_2, R_3, R_4 and R_5 are independently selected from the group of: H and lower alkyl;

(b) said hydrophilic co-monomer has a structure of Formula II:



II

wherein:

Y is O or is absent;

45. The process according to claim 44 or 45, wherein the N-alkyl or N,N-dialkyl substituted acrylamide co-monomer and the hydrophilic co-monomer are the same.

46. The process according to claim 44 or 45, wherein the N-alkyl or N,N-dialkyl substituted acrylamide co-monomer and the hydrophilic co-monomer are different.

47. The process according to claim 45, further comprising mixing said synthetic co-polymer with one or more bioactive agent prior to step (b) and allowing said bioactive agent to cross-link to said synthetic co-polymer through said pendant cross-linkable moiety.

48. The process according to claim 45, further comprising mixing said synthetic co-polymer and said bio-polymer with a plurality of cells in step (b).

49. A synthetic co-polymer produced by the process according to claim 44.

50. A bio-synthetic matrix produced by the process according to claim 45.

51. An ocular implant, comprising:

(a) a synthetic polymer; and

(b) a biopolymer cross-linked to the synthetic polymer, the biopolymer being distributed throughout the implant and being effective to support at least one of cell adhesion and cell growth on the implant when the implant is placed in an eye.

52. The implant of claim 51, wherein the biopolymer is distributed throughout substantially the entire implant.

53. The implant of claim 51, wherein the biopolymer is substantially uniformly distributed throughout the implant.

54. The implant of claim 51, wherein the implant is structured to be placed between a corneal epithelium and a corneal stroma.

55. The implant of claim 51, wherein the implant is a corneal veneer.

56. The implant of claim 51, wherein the biopolymer is cross-linked to the synthetic polymer via a pendant cross-linkable moiety on the synthetic polymer.

57. The implant of claim 51, wherein the synthetic polymer is derived from an acrylamide derivative monomer and the biopolymer comprises a protein component.

58. The implant of claim 57, wherein the acrylamide derivative monomer includes a poly(N-iso-propylacrylamide) component.

59. The implant of claim 57, wherein the protein component includes a collagen component.

60. The implant of claim 51, wherein the implant is a hydrogel.

61. The implant of claim 51, wherein the biopolymer is cross-linked to the synthetic polymer so that each polymer is substantially non-extractable from the implant under physiological conditions.

62. The implant of claim 51, further comprising a bioactive agent located on or in the implant.

63. The implant of claim 51, wherein the implant is shaped as a lens.

64. The implant of claim 63, wherein the implant is shaped as a contact lens.

65. An ocular implant comprising:

(a) a synthetic polymer; and

(b) a bio-polymer cross-linked to the synthetic polymer to form a matrix shaped to be placed on or in a cornea of an eye.

66. The implant of claim 65, wherein the implant is an artificial cornea.

67. The implant of claim 65, wherein the matrix is shaped as a corneal veneer.

68. The implant of claim 65, wherein the matrix is shaped as a lens.

69. The implant of claim 66, wherein the matrix is shaped as a contact lens.

70. The implant of claim 65, wherein the matrix is shaped to be placed between a corneal stroma and a corneal epithelium.

71. The implant of claim 65, wherein the synthetic polymer is derived from at least one acrylamide derivative monomer.

72. The implant of claim 65, wherein the synthetic polymer comprises a co-polymer of three different monomers.

73. The implant of claim 65, wherein the synthetic polymer is derived from an acrylamide derivative co-monomer, a hydrophilic co-monomer, and a carboxylic acid co-monomer.

74. The implant of claim 65, wherein the synthetic polymer is derived from a N-iso-propylacrylamide component.

75. The implant of claim 65, wherein the biopolymer comprises a protein or a carbohydrate effective to facilitate cell growth on the implant.

76. The implant of claim 65, wherein the biopolymer comprises a collagen, or a collagen fragment.

77. The implant of claim 65, wherein the matrix includes a polymer derived from an N-iso-propylacrylamide component, and a protein component.

78. The implant of claim 65, wherein the matrix is a hydrogel.

79. The implant of claim 65, wherein the biopolymer is distributed throughout the implant.

80. The implant of claim 65, wherein the synthetic polymer and bio-polymer are cross-linked together so that each polymer is substantially non-extractable from the implant under physiological conditions and so that at least one of cell adhesion and cell growth is supported on the ocular implant.

81. An ocular implant, comprising:

(a) a lens body structured to be placed on or in a cornea of an eye; and

(b) a bioactive agent cross-linked to a component of the lens body and present in an amount effective to promote nerve growth into the implant.

82. The implant of claim 81, wherein the lens body comprises a synthetic polymer and a biopolymer cross-linked to the synthetic polymer.

83. The implant of claim 82, wherein the biopolymer is cross-linked to the synthetic polymer via pendant cross-linkable moieties on the synthetic polymer.

84. The implant of claim 81, wherein the implant is a corneal veneer.

85. The implant of claim 81, wherein the lens body is structured to be placed between a corneal stroma and a corneal epithelium of an eye.

86. The implant of claim 81, wherein the lens body is structured as a contact lens.

87. The implant of claim 81, wherein the bioactive agent comprises a protein having a nerve cell attachment motif.

88. The implant of claim 81, wherein the bioactive agent comprises a peptide.

89. The implant of claim 88, wherein the peptide has an amino acid sequence YIGSR.

90. The implant of claim 81, wherein the lens body comprises a synthetic polymer and a biopolymer, and the bioactive agent is cross-linked to the synthetic polymer.

91. The implant of claim 81, wherein the bioactive agent is encapsulated in the lens body.

92. The implant of claim 81, wherein the lens body has a refractive index in a range similar to a refractive index of tear film in a human eye.

93. The implant of claim 81, wherein the lens body includes a plurality of pores having diameters in a range from about 140 nm to about 190 nm.

94. The implant of claim 81, wherein the lens body has a glucose diffusion permeability greater than a glucose diffusion permeability of a natural stroma of a human eye.

95. The implant of claim 81, wherein the lens body is optically clear.

96. The implant of claim 81, wherein the lens body comprises a synthetic polymer derived from at least one acrylamide derivative monomer.

97. The implant of claim 81, wherein the lens body comprises a co-polymer of three different monomers.

98. The implant of claim 81, wherein the lens body comprises a synthetic polymer derived from an acrylamide derivative co-monomer, a hydrophilic co-monomer, and a carboxylic acid co-monomer.

99. The implant of claim 81, wherein the lens body is derived from a N-iso-propylacrylamide component.

100. The implant of claim 81, wherein the lens body comprises a protein or a carbohydrate effective to facilitate cell growth on the implant.

101. The implant of claim 81, wherein the lens body comprises a collagen, or a collagen fragment.

102. The implant of claim 81, wherein the lens body includes a polymer derived from an N-iso-propylacrylamide component, and a protein component.

103. The implant of claim 82, wherein the lens body is a hydrogel.

104. The implant of claim 81, wherein the lens body includes a synthetic polymer, and a biopolymer distributed throughout the implant.

105. The implant of claim 104, wherein the biopolymer is distributed throughout substantially the entire implant.

106. The implant of claim 104, wherein the biopolymer is substantially uniformly distributed throughout the entire implant.

107. The implant of claim 81, further comprising living cells located in the lens body.

108. The implant of claim 107, wherein the living cells include ocular cells.

109. The implant of claim 81, further comprising a reinforcement member provided in the lens body.

110. The implant of claim 81, wherein the amount of the bioactive agent is effective to enhance touch sensitivity of the implant after the implant is placed in an eye.